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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,343	01/04/2002	Daniel M. Cimbora	2318-290-II	1043

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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/035,343	Applicant(s) Cimbora et al.
	Examiner Rebecca Prouty	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on Apr 11, 2003.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) 162-182 is/are pending in the application.

4a) Of the above, claim(s) 162, 163, 167, 168, 173, 174, 177, and 180-182 is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) 164-166, 169-172, 175, 176, 178, and 179 is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5,6
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

Claims 1-161 have been canceled. Claims 162-182 are at issue and are present for examination.

Applicant's election without traverse of Group XV, claims 46-52 of the previous restriction requirement and the species of IKK-I and SPA-1 in Paper No. 8 is acknowledged. The previous restriction is herein modified in two ways. First, previously defined groups XV and XVIII are hereby rejoined as they appear to be substantially the same methods merely described in slightly different language and thus are deemed to be patentably indistinct. Second, the previous restriction requirement included compounds identified by the methods of Groups XV/XVIII, XVI, XVII, and XIX-XXII together with the methods. However, in each case the identified compounds are patentably distinct from the methods of identifying their properties as the compounds can be used for other materially different processes such as the purification of the proteins/complexes to which they bind. In response to the previous restriction requirement applicants, elected Group XV (which included a method of identifying compounds and the compounds identified thereby), canceled all previously presented claims and added new claims 161-182. As none of the currently presented claims recite compounds identified by the methods of previous Group XV/XVIII (or any of Groups XVI, XVII, and XIX-XXII) no additional restriction

requirement is necessary herein. However, if applicants present such claims in the future they will be withdrawn as not corresponding to the elected invention, election having been by presentation of only method claims in response to the previous restriction.

Claims 162-163 (corresponding to Group XVII), 167-168, and 177 (corresponding to Group XIX), 173-174 (corresponding to Group XX), and 180-182 (corresponding to Group XXII) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8.

Claims 164, 171 and 175 are objected to because of the following informalities: abbreviations (such as "IKK, LDHM, EIF3S10, SLAP2, KIAA0614, SART1, GBDR1, TRAF, NUMA1, SPA-1 and PN13730") should not be used in the claims without reciting the full terminology for which they are used unless they are common within the art. Furthermore, the space between the N and U in NUMA1 should be deleted. Appropriate correction is required.

Claims 164-166, 169-172 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a determination of the amount of interaction of the first and second proteins in the

absence of the test compound. One of skill in the art cannot determine if a compound alters an interaction without first establishing how much interaction occurs without the compound present.

Claims 170, 172, and 179 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 170, 172, and 179 are indefinite in the recitation of "generating a data set defining one or more selected test compounds" as it is unclear what type of data defines a compound.

Claims 170, 172, and 179 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation of "generating a data set defining one or more selected test compounds, said data set being embodied in a transmittable form" is new matter as nowhere in the specification as filed is such a step disclosed.

Claims 164-166, 169-172, 175-176, and 178-179 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for methods of selecting modulators of an interaction between an IKK-I homolog or variant as recited in the claims and TRAF2, does not reasonably provide enablement for methods of selecting modulators of an interaction between any IKKA, IKKB, IKKG or IKK-I homolog as recited in the claims and any LDHM, EIF3S10, SLAP2, KIAA0614, SART1, GBDR1, TRAF, NUMA1, SPA-1 OR PN13730. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's specification used yeast two-hybrid screens of a human brain cDNA library with portions of IKKA, IKKB, IKKG and IKK-I as bait to identify human proteins which will bind to these proteins. While each of IKKA, IKKB, IKKG or IKK-I have well defined roles in the activation of the NFκB signal transduction system and the usefulness of modulators of the NFκB signal transduction system is well established in the art, the specification fails to show that any of the binding pairs claimed is physiologically relevant (i.e., occurs *in vivo*) during activation of the NFκB signal transduction system. Cao, US Patent 5,776,717, teaches that the IKK-I/TRAF2 interaction is in fact a physiologically relevant interaction. It is well

established in the art that many kinases can bind to and phosphorylate a wide variety of substrates *in vitro* that they do not appear to have any *in vivo* interaction with. The presence of an *in vivo* interaction requires colocalization of the two binding partners within the same cell and subcellular space at some time. However, the two-hybrid screen merely tests whether two proteins can bind to one another if these conditions are met. It fails to in any way suggest whether such interaction actually reflects any physiological situation. Furthermore, the specification provides evidence that only some of the binding interactions encompassed by the instant claims can even occur *in vitro* as many pairs encompassed were not in fact found in the yeast two hybrid screen described. As such one of skill in the art would have no expectation that any compounds which would be selected by the claimed methods would be useful for modulating the NFκB signal transduction system as there is no evidence that the binding of any of these pairs is in fact part of the NFκB signal transduction system and it would require undue experimentation to determine how to use compounds selected by the claimed methods.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the

> prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 164-166, 169-172, 175-176, and 178-179 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cao (US Patent 5,776,717) or Akira et al (WO 00/24908).

Cao teach that a family of IKKs that phosphorylate IκB molecules on the specific regulatory serine residues. This family is disclosed to comprise the KIAA0151 gene product (which is identical in amino acid sequence to IKK-I as evidenced by GenBank entry D63485). The members of this family, including specifically the KIAA0151 gene product, are disclosed to bind to TRAF2 (see column 6, lines 59-65). Cao further teach methods for identifying agents which modulate IκB kinase cellular functions, including binding to a IKK binding target (see column 4, lines 47-56). These methods comprise mixing an IκB kinase, such as the KIAA0151 gene product, which may be part of a fusion protein with

a tag peptide and a binding target of the kinase protein (such as TRAF2) in the presence and absence of a candidate modulator and detecting the amount of binding between the IKK and its binding target (see particularly column 5). Cao do not specifically teach the selection of the KIAA0151 gene product as the IκB kinase and TRAF2 as the IKK binding target for use in the disclosed methods. However, the selection of these two proteins as the binding partners in the disclosed methods would have been obvious to one of ordinary skill in the art as Cao teach that TRAF2 is the protein that directly links activation of the TNF pathway with activation of the NFκB signal transduction system and thus one of skill in the art would expect modulators of the interaction of TRAF2 with a direct activator of the NFκB signal transduction system such as the KIAA0151 gene product would be useful for modulating inflammatory diseases as taught by Cao. It would be further obvious to the skilled artisan to determine the structure of a compound which is capable of modulating the interaction and to store data regarding this structure on a computer disc.

Akira et al. (see US Patent Application Publication 2003/005419 for an English translation) teach the IκB kinase IKK-I, that this IκB kinase specifically interacts with I-TRAF, and that this interaction is important for regulating apoptosis (see

paragraphs 70 and 122). Akira et al. further teach methods for detecting binding of IKK-I and I-TRAF which comprise mixing a fusion of IKK-I to a FLAG tag and a fusion of I-TRAF to a Myc epitope, immunoprecipitating with an anti-FLAG antibody and measuring the amount of I-TRAF by means of Western blotting with an anti-Myc antibody or alternatively immunoprecipitating with an anti-Myc antibody and measuring the amount of IKK-I by means of Western blotting with an anti-FLAG antibody. Akira et al. do not specifically teach screening for compounds which modulate this binding interaction. However, it would have been obvious to one of ordinary skill in the art to test for modulators of this interaction by detecting binding between IKK-I and I-TRAF as taught by Akira in the presence and absence of a potential modulator in order to find compounds useful for treating apoptosis related diseases. It would be further obvious to the skilled artisan to determine the structure of a compound which is capable of modulating the interaction and to store data regarding this structure on a computer disc.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy,

can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652